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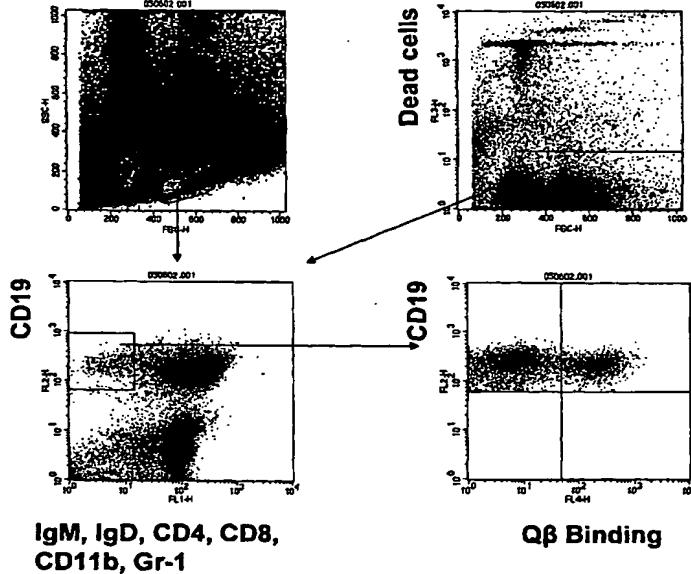
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Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: SELECTION OF B CELLS WITH SPECIFICITY OF INTEREST: METHOD OF PREPARATION AND USE



(57) Abstract: The present invention is related to the fields of molecular biology, virology, immunology and medicine. The invention provides methods using a composition comprising an ordered and repetitive antigen or antigenic determinant array for visualization and selection of B cells specific for the antigen. These B cells are useful for the production of monoclonal antibodies used for therapy, diagnostic or research purposes.

WO 2004/102198 A3



EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

— of inventorship (Rule 4.17(iv)) for US only

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INTERNATIONAL SEARCH REPORT

International Application No PCT/EP2004/005208	
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A. CLASSIFICATION OF SUBJECT MATTER			
IPC 7	G01N33/566	G01N33/569	G01N33/50
			C07K16/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	-/-	

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

*** Special categories of cited documents :**

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the International filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the International filing date but later than the priority date claimed

T later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

29 October 2004

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26.11.04

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Montrone, M

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/005208

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: 58 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple Inventions in this International application, as follows:

see additional sheet

As a result of the prior review under R. 40.2(e) PCT,
no additional fees are to be refunded.

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1,2,5,10-46,49,54 to 62(all partially),7-9,51-53(all complete)

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the Invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 58

Present claim 58 relates to a product defined by reference to a desirable characteristic or property, namely the selection of said cells by the method of claim 1. This claim falls clearly under the so called "reach through" claim format facing severe problems with respect to Article 6 PCT and Article 33(2) PCT since it is not clear which cells fall under the scope of protection of such a claim and whether already known antigen-specific B cells are not detrimental to novelty of such a claim. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/005208

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WEITKAMP JORN-HENDRIK ET AL: "Generation of recombinant human monoclonal antibodies to rotavirus from single antigen-specific B cells selected with fluorescent virus-like particles." JOURNAL OF IMMUNOLOGICAL METHODS, vol. 275, no. 1-2, 1 April 2003 (2003-04-01), pages 223-237, XP004416763 ISSN: 0022-1759 abstract page 224, column 2, paragraph 2 - page 225, column 2, paragraph 2; figure 1 page 226, column 1, paragraphs 1,2 page 226, column 2, paragraph 3 - page 227, column 2, paragraph 2 page 235, column 1, paragraph 3 - page 236, column 1, paragraph 2	1,2, 12-36, 43,58, 61,62
Y		5,7-11, 37-42, 44-46, 49, 51-57, 59,60
A	WO 03/024481 A (BACHMANN MARTIN F ; LIPOWSKY GERAD (CH); MAURER PATRICK (CH); MEIJERIN) 27 March 2003 (2003-03-27) abstract page 6, paragraph 1 page 26, paragraph 4 - page 28, paragraph 4 page 36, paragraph 3 - page 38, paragraph 2 page 39, paragraph 2 - page 50, paragraph 1	1,2, 10-46, 54-62
Y	FEHR T ET AL: "T cell-independent type I antibody response against B cell epitopes expressed repetitively on recombinant virus particles" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 95, no. 16, 4 August 1998 (1998-08-04), pages 9477-9481, XP002212229 ISSN: 0027-8424 abstract page 9477, column 2, paragraphs 1,2 page 9480, column 2, paragraphs 1,2	5,7-11, 37-42, 44-46, 49, 51-57, 59,60
		-/-

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/005208

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	VASILJEVA I ET AL: "Mosaic Qbeta coats as a new presentation model" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 431, no. 1, 10 July 1998 (1998-07-10), pages 7-11, XP004258931 ISSN: 0014-5793 abstract page 7, column 1, paragraph 1 - column 2, paragraph 1 page 10, column 1, paragraph 1	5,7-11, 37-42, 44-46, 49, 51-57, 59,60
Y	JEGERLEHNER A ET AL: "A molecular assembly system that renders antigens of choice highly repetitive for induction of protective B cell responses" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 20, no. 25-26, 19 August 2002 (2002-08-19), pages 3104-3112, XP004374549 ISSN: 0264-410X abstract page 3104, column 2, paragraph 2 - page 3105, column 1, paragraph 1 page 3111, column 1, paragraph 2	5,7-11, 37-42, 44-46, 49, 51-57, 59,60
Y	BACHMANN M F ET AL: "The influence of virus structure on antibody responses and virus serotype formation" IMMUNOLOGY TODAY, ELSEVIER PUBLICATIONS, CAMBRIDGE, GB, vol. 17, no. 12, 1 December 1996 (1996-12-01), pages 553-558, XP004071007 ISSN: 0167-5699 abstract page 553, column 1, paragraph 1 - column 2, paragraph 1 page 557, column 2, paragraph 5	5,7-11, 37-42, 44-46, 49, 51-57, 59,60
Y	US 5 326 696 A (CHANG TSE W) 5 July 1994 (1994-07-05)	5,7-11, 37-42, 44-46, 49, 51-57, 59,60
	abstract column 4, line 58 - column 6, line 15 column 9, lines 38-60 column 12, lines 30-66	
		-/-

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/005208

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BENHAR I: "Biotechnological applications of phage and cell display" BIOTECHNOLOGY ADVANCES, ELSEVIER PUBLISHING, BARKING, GB, vol. 19, no. 1, 1 February 2001 (2001-02-01), pages 1-33, XP004231501 ISSN: 0734-9750 abstract page 21, paragraph 2 - page 23, paragraph 1 -----	1,2,5, 7-46,49, 51-62

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 03024481	A 27-03-2003	EP 1450856	A2 01-09-2004	
		WO 03024481	A2 27-03-2003	
		US 2003099668	A1 29-05-2003	
US 5326696	A 05-07-1994	US 5213960	A 25-05-1993	
		US 5256542	A 26-10-1993	
		AU 3785493	A 05-10-1993	
		WO 9318068	A1 16-09-1993	